REMARKS/ARGUMENTS

Status of the Claims

Claims 71, 76, 77, 79, and 80 were rejected. Claims 1-70, 72-75, and 78 were previously canceled without prejudice or disclaimer. Applicants expressly reserve the right to file a continuation or divisional application or to take other such appropriate action to seek protection of the canceled subject matter. To expedite prosecution, claims 71, 76, 77, 79, and 80 have been amended to delete the term "discrete" dried particles and to correct a minor typographical error in claims 76, 77, 79, and 80, as set forth in more detail below. No new matter has been added by way of the claim amendments.

Claims 71, 76, 77, 79, and 80 are now pending in the present application. Reexamination and reconsideration of the claims are respectfully requested in view of the claim amendments and the following remarks. The Examiner's rejections in the Office Action are addressed below in the order set forth therein.

The Rejection of the Claims Under 35 U.S.C. § 103 Should Be Withdrawn

Claims 71, 76, 77, 79, and 80 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Application Publication No. 2002/0120228 (hereinafter "the '228 publication") in view of U.S. Patent Application Publication No. 2006/0024322 (hereinafter "the '322 publication"). As noted above, claims 71, 76, 77, 79, and 80 have been amended. This rejection is respectfully traversed as to the pending claims.

Independent claim 71 as previously presented was drawn to a particulate recombinant Staphylococcal enterotoxin B (rSEB) vaccine composition comprising discrete dried particles, wherein at least about 50% of the discrete dried particles have a volume diameter within 80% of the mean. Dependent claims 76, 77, 79, and 80 further recited specific ranges for particle volume mean diameter and particle mean aerodynamic diameter. To expedite prosecution, the rejected claims have been amended to delete the term "discrete" dried particles, as described in greater detail below. The Examiner maintains that these claims are obvious in view of the '228 publication and the '322 publication. The present obviousness rejection will be addressed insofar as it may apply to the amended claims.

The '228 publication discloses a gel-forming, free-flowing powder suitable for use as a vaccine, prepared by a spray-drying or spray-freeze-drying process. The Examiner concludes that the particles of the '228 publication "necessarily encompass at least 50% of the resultant population of discrete dried particles and have a volume diameter within 80% of the mean." Page 4, Office Action mailed June 25, 2008. Applicants note that the Examiner has not provided any evidence to support this broad conclusory statement. Furthermore, as acknowledged by the Examiner, the '228 publication does not teach or suggest an rSEB vaccine composition. See page 7, Office Action mailed June 25, 2008.

The '322 publication is directed to rSEB vaccines for the treatment of autoimmune diseases, particularly a solid vaccine formulation produced by *lyophilization*. See paragraph [0048] of the cited reference. As indicated previously, the process of lyophilization produces an rSEB vaccine "cake" rather than a collection of rSEB vaccine particles having a uniform size distribution, as described in the instant specification and recited in the claims. The Examiner, however, concludes that the teachings of the '228 publication and the '332 publication can be combined to arrive at the claimed particulate rSEB vaccine compositions. Applicants respectfully disagree with the Examiner's conclusions.

Establishing a *prima facie* case of obviousness requires assessment of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), which provides the framework for applying the statutory language of § 103. Under the "Graham Factors," the Examiner is required to:

1. Determine the scope and content of the prior art;
2. Ascertain the differences between the prior art and the claims at issue;
3. Resolve the level of ordinary skill in the pertinent art; and
4. Consider any relevant secondary considerations.

Furthermore, a *prima facie* case of obviousness under 35 U.S.C. § 103(a) requires that a reference in combination with one or more additional references places the claimed subject matter in the public domain prior to Applicants' date of invention. See *In re Zenitz*, 333 F.2d 924, 142 USPQ 158 (C.C.P.A. 1964). Thus, establishing a *prima facie* case of obviousness requires that the cited references can be combined such that each and every element of the claimed invention is taught, explicitly or implicitly, by the references and that a reasonable

expectation of success exists in such a combination. In the instant case, neither of the cited references, alone or in combination, discloses a particulate rSEB vaccine composition comprising dried particles, *wherein at least 50% of the dried particles have a volume mean diameter within about 80% of the mean.* Here, the cited references do not teach or suggest the recited claim element of a particulate rSEB vaccine composition comprising dried particles having a uniform size distribution (i.e., at least 50% of the dried particles have a volume mean diameter within about 80% of the mean). In fact, the Applicants of the '228 publication explicitly state that "[t]he average particle size of the powders according to the present invention can vary widely." See paragraph, for example, page 4, paragraph [0058]. Moreover, as the lyophilization methods taught by the '322 publication produce a dried vaccine "cake," this reference also necessarily does not disclose an rSEB vaccine composition comprising discrete dried vaccine particles, wherein at least 50% of the particles have a volume diameter within about 80% of the mean, as recited in all of the pending claims. Thus, contrary to the Examiner's assertion on page 4 of the present Office Action, the '322 publication does not cure the deficiencies of the '228 publication, and a *prima facie* case of obviousness has not been established.

Although Applicants maintain that a *prima facie* case of obviousness has not been established in the present case, evidence of secondary considerations such as unexpected results or unforeseen advantageous properties of the claimed particulate rSEB vaccine composition can rebut a *prima facie* case of obviousness. See *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987); *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Claim 71 and all claims dependent thereon recite a particulate rSEB vaccine composition having a well-defined particle size distribution (i.e., "wherein at least about 50% of the dried particles have a volume diameter within about 80% of the mean"). Vaccine compositions comprising a population of dried solid particles that display a well-controlled, uniform particle size distribution are advantageous for a number of reasons. Uniform particle size of the vaccine composition reduces the potential for particle agglomeration, thereby facilitating accurate dosing to patients when the vaccine composition is administered intranasally as a powder or intradermally following reconstitution of the particulate vaccine composition in a pharmaceutically acceptable carrier. In

the exemplary case of intranasal delivery of a vaccine composition of the invention, the well-controlled particle size range recited in the claims permits the adherence of the particles to the nasal lining or sinuses, where the vaccine particles are rapidly absorbed into the bloodstream, and minimizes delivery of the composition into the pulmonary system where it may cause negative, unwanted side effects. The accurate intranasal targeting of the claimed rSEB vaccine also reduces the time required to mount an effective antibody response. Applicants respectfully remind the Examiner that the secondary consideration of unexpected or superior results obtained with an invention provides objective indicia of nonobviousness. See, for example, *In re Mayne*, 104F.3d 1339, 1342, 41USPQ2d 1451, 1454 (Fed. Cir. 1997) and *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990). Such secondary considerations further support the conclusion that the rejected claims are not obvious.

And finally, the Examiner concludes that the vaccine particles of the '228 publication fall within the particle size distribution recited in the present claims and further states that the particles of the cited reference "would necessarily be more uniform in size" because "the diameter range [of the particles of the '228 publication] is narrower than that of the instant invention." Page 4, Office Action mailed June 25, 2008. Applicants first note that the Examiner has made these broad statements without providing any evidence to support them. Moreover, the diameter range of the particles of the '228 publication "can vary widely and is generally from 0.1 to 250 μm." Paragraph [0058]. Therefore, contrary to the Examiner's assertions, the diameter range recited in the dependent claims is actually *narrower* than that of the cited reference (i.e., 35 μm – 300 μm v. 0.1 μm to 250 μm). In addition, Applicants maintain that recitation of a "narrow" particle size range, depending on the chosen definition of "narrow," does not necessarily indicate a uniform particle size distribution, as the Examiner appears to argue. Accordingly, Applicants respectfully submit that the Examiner has not provided sufficient evidence to demonstrate that the vaccine particles of the '228 publication (or the '322 publication) fall within the well-defined particle size distribution set forth in the instant claims (i.e., "wherein at least about 50% of the dried particles have a volume diameter within about 80% of the mean"), thereby providing additional evidence of the nonobviousness of the claims.

In view of the above remarks and the secondary considerations of nonobviousness, Applicants respectfully maintain that the claims are not obvious and request that the rejection of claims 71, 76, 77, 79, and 80 under 35 U.S.C. § 103(a) in view of the '228 publication and the '322 publication be withdrawn.

The Objection to the Claims Should Be Withdrawn

Claims 76, 77, 79, and 80 were objected to for recitation of the abbreviation "μM" instead of "μm" in reference to micrometers. Applicants appreciate the Examiner bringing this to their attention and have amended the claims to correct this typographical error. No new matter has been added by way of the claim amendments. Applicants respectfully submit that the objection to claims 76, 77, 79, and 80 has been obviated and should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

New Matter

Claims 71, 76, 77, 79, and 80 were rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. In particular, the claims have been rejected for recitation of the phrase "*discrete* dried particles," which the Examiner maintains lacks adequate support in the originally filed application. Although Applicants do not concede the accuracy of the Examiner's assertion, the term "discrete" has been deleted from the claims to expedite prosecution. In light of this amendment, the rejection of the claims under 35 U.S.C. § 112, first paragraph, has been obviated and should be withdrawn.

The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 71, 76, 77, 79, and 80 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Specifically, the Examiner maintains that the claim language "*discrete* dried particle" is unclear because this phrase is not explicitly defined in the specification. See page 9, Office Action mailed June 25, 2008. As discussed above, the claims

have been amended to delete the word "discrete." Therefore, Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 112, second paragraph.

CONCLUSION

The Examiner is respectfully requested to withdraw the rejection of claims 71, 76, 77, 79, and 80. In view of the above remarks and the claim amendments, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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